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| 10/630,180 | 07/30/2003 | Zheng Wei | 10709/47 | 9214 |

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| EXAMINER | |
|---|---|
| DEBERRY, REGINA M | |

| ART UNIT | PAPER NUMBER |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/630,180 | WEI, ZHENG | |
| | Examiner | Art Unit | |
| | REGINA M. DEBERRY | 1647 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-26,28-53,61,62 and 65-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26,28-53,61,62 and 65-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 31 October 2007 has been entered.

### *Status of Application, Amendments and/or Claims*

The amendment filed 31 October 2007 has been entered in full. Claims 27, 54-60, 63, 64 and are canceled. New claims 65-70 are added. Claims 1-26, 28-53, 61, 62, 65-70 are under examination.

### *Information Disclosure Statement*

The information disclosure statement(s)(IDS) filed 09 January 2008 was received and complies with the provisions of 37 CFR §§1.97 and 1.98. It has been placed in the application file and the information referred to therein has been considered as to the merits.

### *Withdrawn Objections And/Or Rejections*

The rejection to claims 27 and 54 under 35 U.S.C. 112, First paragraph, Written description, New Matter, as set forth at pages 6-8 of the previous Office Action (14 August 2007), is *withdrawn* in view of the amendment (31 October 2007).

The rejection to claims 27, 63 and 64 under 35 U.S.C. 112, second paragraph, as set forth at pages 8-9 of the previous Office Action (14 August 2007), is *withdrawn* in view of the amendment (31 October 2007).

**Claim Rejections-35 USC § 112, Second Paragraph**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-26, 28-62, 65-70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-26, 28-62, 65-70 are rejected because of the interchangeable use of "monitoring movement" and "assaying movement" (see claims 1, 28, 66, 69). The difference between the claim limitations is unclear and thus the metes and bounds of the instant claims cannot be determined.

Claim 66 is indefinite because the method is drawn to a "first population comprising the first selected chemoattractant receptor" and a "second population comprising the second selected chemoattractant receptor". However, claim 66 depends from claim 1, which recites **a single population expressing two different chemoattractant receptors.** Claim 66 is indefinite because it depends from a claim (claim 1) drawn to only one cell population with two receptors, thus it is unclear what is exactly be examined in claim 66. The metes and bounds of the instant claim cannot be determined.

**Claim Rejections-35 USC § 112, First Paragraph, Enablement**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-26, 28-53, 61, 62 (and new claims 65-68, 70) remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The basis for this rejection is set forth at pages 2-6 of the previous Office Action (14 August 2007).

Applicant asserts that the specification fully enables the scope of claims 1 and 28 and any claims dependent thereon for the following reasons. Applicant argues that the specification, provides ample description of the BiRAM assay for use in identifying non-specific candidate antagonist hits to the chemoattractant receptors selected for use in the assays. Applicant cites pages in the instant specification. Applicant cites pages 39-43 and Examples 8-10, for specific examples of the BiRAM screening assay. Applicant contends that the skilled artisan, provided the guidance in the specification, would understand how to use BiRAM assays to identify antagonist hits to the selected chemoattractant receptors used in those assays. Applicant points out that, as amended, claims 1 and 28 do not require that the identity of the chemoattractant receptor reacting in the BiRAM assay is known at the end of the BiRAM assays.

Applicant's arguments have been fully considered but are not deemed persuasive. The specification teaches that the reverse activation of migration (RAM) assay identifies and discriminates antagonists while decreasing the prevalence of false

positives and negatives signals found in other assays. The specification teaches that conventional screens for antagonists of cell migration measure the reduction of cell migration; the RAM assay measures the activation of cell migration. In the RAM assay, cells are challenged to migrate in the presence of migration-inhibitory concentrations of chemoattractants in response to candidate antagonists. The purported novelty of the instant invention is that the RAM assay identifies and discriminates antagonists while decreasing the prevalence of false positives and negatives signals found in other assays using set parameters. Ligands induce cell migration, but at inhibitory concentration certain ligand inhibits cell migration. The specification teaches that when a cell migrates in the presence of a candidate antagonist and an inhibitory concentration of the ligand, the candidate antagonist is identified as a true antagonist. In the RAM assay, cells are challenged to migrate in the presence of migration-inhibitory concentrations of chemoattractants in response to true antagonists.

The specification teaches that in a binary RAM (BiRAM) assay, two types of chemoattractant receptors can be assayed in the same assay. Either a single cell population comprising two different receptors on one cell or two distinct cell populations each comprising a different receptor are incubated with a candidate antagonist and then contacted with an inhibitory concentration of ligands for the target receptor. The ability of the cell populations to migrate in response to treatment with a candidate antagonist is assayed. If the cell migrates in the presence of a candidate antagonist, then a positive signal is observed (page 12, lines 1-10; page 18, lines 5-21 and page 19, line 1-page 20, line 30). The specification states that the BiRAM screening assay identifies hits,

which correspond to either of the chemokine receptors present on the population of cells used in the screening assay. The specification states that although the hits may identify an antagonist to one or more chemokine receptors, the identity of this chemokine receptor(s) reacting in the assay and causing cell migration is not known at this stage of the assay. The specification states that because the hit rate is very low, *i.e.* less than 1%, receptors identity can be then determined by re-screening the candidate antagonist in a RAM assay in which only one chemokine is applied at a time (page 20, lines 5-15).

The instant claims are not enabled for the following reasons. The Examiner will break down the reasons why the particular claims are not enabled.

Claims 1-26, 28-53, 61, 62, 65, 67, 68 and 70 are not enabled because the specification fails to teach how to use a chemoattractant antagonist if the identity of its chemoattractant receptor is not identified in the BiRAM assay. Applicant argues that as amended, claims 1 and 28 do not require that the identity of the chemoattractant receptor reacting the in BiRAM assay is known at the end of the assay. This is not found persuasive. One of the purported utilities of the BiRAM assay is to identify chemoattractant receptor antagonists of chemoattractant receptors that could possibly be used in drug development. **The specification does not teach *how to use* an antagonist to an unknown/unidentified chemoattractant receptor.** It is unclear how the skilled artisan would use an antagonist without knowing the chemoattractant receptor to which it binds. It is unclear how drugs would be developed without knowing the possible affects on its binding receptor.

In addition, claims 1-26, 61, 65-67 are not enabled because the specification fails to teach how to identify candidate antagonists and the chemoattractant receptors causing the cell migration when the BiRAM assay employs two different chemoattractant receptors on the same cell and at least two candidate antagonists. When a single cell population comprising two different chemokine receptors is incubated with candidate antagonists in the upper chamber, how does one skilled in the art discern *which chemoattractant receptor and which candidate antagonist* is inducing the single cell population to migrate to the lower chamber. Contrary to Applicant's assertion, the instant examples employ **known antagonists to known chemoattractant receptors**. The instant examples **do not teach** the incubation of ***candidate antagonist (i.e. unknown antagonists)*** together with a single cell population comprising two different chemoattractant receptors in the upper chamber, wherein incubation induces cell population migration to the lower chamber in the presence of inhibitory concentrations of ligands of the two different chemoattractant receptors wherein the candidate antagonist(s) is identified as a true antagonist and its chemoattractant receptor(s) is identified. The teachings in the examples are not tantamount to the instant claims.

Only new claim 69 recites a method that could identify an antagonist to two different cell populations each comprising a different chemoattractant receptor **by re-screening the candidate antagonist in a RAM assay in which only one chemokine and one cell population is applied at a time.** However, this method is not applicable to one cell population comprising two different chemoattractant receptors (i.e. claim 66).

Due to the large quantity of experimentation necessary to identify a candidate antagonist(s) as a true antagonist and its chemoattractant receptor(s) and the large quantity of experimentation necessary to employ a chemoattractant antagonist to an unknown/unidentified chemoattractant receptor, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which fail to recite limitations regarding parameters for identifying unknown candidate antagonists and its chemoattractant receptors on single cell populations and employing unknown chemoattractant antagonists, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

**It is noted that if the limitations of claims 68 and 69 were put in claim 28; claim 28 (and those claims dependent on claim 28) would be allowable.**

Thus, if claim 28 was amended to recite:

"A method for identifying an antagonist of at least one of selected first and second chemoattractant receptors antagonist, comprising:

a) providing an apparatus comprising an upper chamber and a lower chamber separated by a porous membrane; i) placing a candidate antagonist and a first cell population and a second cell population in the upper chamber, wherein the first cell population comprises the first selected chemoattractant receptor and wherein the second cell population comprises the second selected chemoattractant receptor; ii) placing an inhibitory concentration of a ligand for the first selected chemoattractant receptor in the lower chamber; placing an inhibitory concentration of a ligand for the

second selected chemoattractant receptor in the lower chamber; and iii) monitoring movement of the first and the second cell populations from the upper chamber to the lower chamber, wherein the movement identifies the candidate antagonist as an antagonist of at least one of the first and second selected chemoattractant receptors;

further comprising a step of determining whether an identified antagonist is an antagonist for one of the first selected chemoattractant receptors, the second selected chemoattractant receptor, or both;

b) wherein determining is performed by a method comprising the steps of: determining whether the identified antagonist is the antagonist for the first selected chemoattractant receptor comprising the steps of: i) placing a first cell population comprising the first selected chemoattractant receptor and a candidate antagonist in the upper chamber, ii) placing an inhibitory concentration of a ligand for the first selected chemoattractant receptor in the lower chamber, and iii) monitoring movement of the first cell population from the upper chamber to the lower chamber, wherein the movement identifies the candidate antagonist as an antagonist of the first selected chemoattractant receptor; and

c) determining whether the identified antagonist is the antagonist for the second selected chemoattractant receptor comprising the steps of: i) placing a second cell population comprising the second selected chemoattractant receptor and the candidate antagonist in the upper chamber, ii) placing an inhibitory concentration of a ligand for the second selected chemoattractant receptor in the lower chamber, and iii) monitoring movement of the second cell population from the upper chamber to the lower chamber,

wherein the movement identifies the candidate antagonists as an antagonist of the second selected chemoattractant receptor."

**It is also noted that if Applicant can demonstrate (using support from the instant specification), how one skilled in the art can distinguish between 2 different chemoattractant receptors on the same/single cell population (i.e. the identity of the receptor reacting in the BiRAM assay and causing cell migration) and the limitations of claims 65 and 66 were put in claim 1; claim 1 (and those claims dependent on claim 1) would be allowable.**

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to REGINA M. DEBERRY whose telephone number is (571)272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Marianne P. Allen/
Primary Examiner, Art Unit 1647

RMD
1/30/08